Toxoplasmosis in humans: discussion paper

D O Ho-Yen MRCPath MD *Scottish Toxoplasma Reference Laboratory, Raigmore Hospital, Inverness IV2 3UJ*

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Toxoplasmosis in humans has developed through several stages. In the past, it was regarded as a minor infection but extensive media attention in the late 80s has made the general public aware of this infection. Hopefully, the 90s will be a decade in which the medical and scientific communities will appreciate the growing importance of *Toxoplasma gondii* infection in humans.

Congenital infection

Television, radio and newspaper items have succeeded in creating high public awareness of this condition. The registered charity, 'Toxoplasma Trust' for parental groups was formed in 1989 with the objectives of 'increasing public awareness of this condition' and 'establishing an antenatal screening programme' for pregnant women. Although there is a strong, emotional argument for screening, it is still important to consider carefully the cost-benefit and implications of screening to the National Health Service.

A compulsory screening programme is in operation in France and Austria. Several other European countries are seriously considering introducing similar programmes. However, the seroprevalence in Britain is different: approximately 20% of pregnant women are susceptible at the start of pregnancy in France, whereas in Britain, the figure is 80%[1]. Thus, a screening programme in Britain entails follow-up during pregnancy of more women. In Scotland, it is estimated that there is a primary infection in 2/1000 pregnancies, transmission of infection to the fetus in 50% and most maternal infections may be asymptomatic[2]. If women are tested three times in pregnancy (antenatal booking, 2nd trimester and at parturition), with in-house reagents and results being confirmed by Reference Laboratories, screening is of cost-benefit[3]. Even when other factors are considered such as psychological costs, health education and administration of the scheme there appears to be a strong case for screening[4].

Parental groups must recognize that a screening programme is not necessarily a panacea. Some women will be made aware of a risk to their pregnancy that they did not perceive. Those who are susceptible will have to be given health education to avoid infection. Cat faeces are the principal source of infection and pregnant women should avoid cleaning cat litter trays. If this cannot be avoided, cleaning should be done daily. Hands should be washed carefully after contact with potential sources of infection such as litter trays, sand pits, soil and uncooked meat. Undercooked meat and unpasteurized milk should not be consumed. Women who become infected will have further investigations to establish if the fetus is infected. Infected fetuses require more toxic therapy and not all congenital abnormalities can be prevented with treatment. Nevertheless when all of these factors are considered, the potential value of a screening programme is probably still greater than the disadvantages. When primary infection in the mother is suspected, she is started on spiramycin 750 mg four times a day. Confirmation that the fetus is infected requires the treatment regimen given in Table 1. The baby is assessed at birth, but 90% will be asymptomatic and the toxoplasma triad (choroidoretinitis, hydrocephalus and intracerebral calcification) will only affect a few babies. Unfortunately eye symptoms may develop up to 18 years later[7] and so all infected neonates require treatment as in Table 1.

Table 1. Treatment of primary infection in mother[5] and neonates[6]

	Mother	*Neonate*
(i) Spiramycin	750 mg (×4/day)	50 mg/kg (×2/day)
(ii) Sulphadiazine	3 g/day	50 mg/kg (×2/day)
Pyrimethamine	50 mg/day	1 mg/kg (×2/week)
Folinic acid	6 mg/day	5 mg (×2/week)
		(Corticosteroids)

Alternate (i) and (ii) every 3-5 weeks

Table 2. Acquired toxoplasma infection

Healthy
Asymptomatic (primary/reactivation)
Pyrexial illness (primary/reactivation)
Eye complaints (primary/reactivation)
Infectious-mononucleosis-like illness (primary)
Myalgic encephalomyelitis (primary)
Immunocompromised
Asymptomatic (primary/reactivation)
Pyrexial illness (primary/reactivation)
Disseminated infection (primary/reactivation)

Acquired infection

A variety of factors in modern living can produce an increase in toxoplasma infections. Changes in eating habits with greater consumption of undercooked meat or unpasteurized goat's milk may produce more infection among the healthy. Medical practice is also resulting in more individuals with suppressed immune systems either because of aggressive

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treatment of disease or associated with organ transplantation. In addition, certain patterns of human behaviour, such as homosexuality or drug misuse, may result in immunocompromise by acquisition of infection, especially the human immunodeficiency virus (HIV). Acquired infection is understandably less severe in the healthy compared to those who are immunocompromised. The spectrum of acquired infection is shown in Table 2.

Healthy individuals

Most infections are asymptomatic or non-specific, pyrexial illnesses. Eye complaints are usually associated with reactivation of congenital infection, but less commonly, they may present as primary infection. The most common clinical manifestation of *T. gondii* in healthy individuals is an infectious mononucleosis-like illness. It can be difficult to differentiate such illnesses from classical, Epstein-Barr virus infectious mononucleosis as significant atypical lymphocytes may be present[8]. All patients with Epstein-Barr virus negative serology should be tested for evidence of toxoplasma infection.

The likelihood of toxoplasma infection increases with age, perhaps because there is an increased cumulative exposure to infection as one gets older. Therefore, infection as a result of travel abroad and consumption of undercooked meat or unpasteurized milk is more likely. Certain groups in Britain are also at increased risk of infection, for example those individuals who consume unpasteurized goat's milk. For some, goat's milk is believed to be a health food whereas others may have their own goats. There is one family in which both the children acquired infection, but their parents did not, from consuming their own goat's milk[9]. The explanation was probably that the children had glass-fulls of fresh goat's milk whereas the parents only had goat's milk in coffee or tea where the temperature was sufficient to kill the organism.

Convalescence after infectious mononucleosis may be prolonged, as it can be with toxoplasmosis. I have found in a study of 50 patients who could fulfil the criteria of post viral fatigue syndrome[10] (PVFS, myalgic encephalomyelitis) that two had evidence of initiating toxoplasma infection. The incidence of PVFS appears to be increasing and it is certainly likely that, because of changing behaviour, some of these individuals may have toxoplasmosis. From the few individuals with toxoplasmosis mistaken for PVFS who have been monitored, it seems that the prognosis is much better in those with a diagnosis of toxoplasmosis.

Immunocompromise

Immunocompromise makes an individual more susceptible to infections, including toxoplasmosis. It seems that with immunocompromise, there is a greater likelihood of severe primary toxoplasmosis; and when there is severe immunocompromise, reactivation of past toxoplasma infection is also more likely. For many conditions, such as autoimmune disease or malignancy, medical treatment now involves immunosuppression. In addition, there has been a dramatic increase in the last decade of organ transplantation which may necessitate severe immunosuppression. Thus, toxoplasmosis has been associated with renal, heart, heart-lung and bone marrow transplantation. If there is a mis-matched transplant (donor organ infected, recipient susceptible), there is a strong possibility of primary infection and it seems wise to give prophylactic pyrimethamine 25 mg/day for 6 weeks[11] or to avoid mis-matches. When there is severe immunosuppression, especially with an anti-T-cell component[12], reactivation is likely and such patients may also benefit from prophylactic therapy.

Infections may by themselves produce immunocompromise, especially human immunodeficiency virus infection. Such cases have been particularly associated with disseminated infection and cerebral toxoplasmosis[13]. Unfortunately, in these patients, as they do not readily produce the usual antibody response, diagnosis can be particularly difficult. There is a need for the development of better antigen detection tests, such as the polymerase chain reaction, or, the adoption of more sophisticated antibody tests such as Western blotting. Until these become a reality, many patients will have to be treated empirically on the basis of a clinical diagnosis. For the 1990s the diagnosis and prevention of toxoplasma infections are growing problems which require answers.

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